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Review on Formulation Approaches and Evaluation Parameters of Mouth Dissolving Tablet

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ABSTRACT

Since the past decade, oral administration has received substantially more attention for the treatment or management of disorders. Mouth dissolving tablets (MDTs), a novel idea in oral delivery, are now widely used. Mouth dissolving tablets are solid dosage forms that dissolve and release the active ingredient when placed in the mouth for a short period of time without the use of water. Geriatric, paediatric, and bedridden patients are particularly affected by it since they have swallowing issues, like those with dysphasia. This article discusses the various excipients evaluation tests, marketed formulations, and drugs used in his research area, along with the many formulation aspects and technologies developed for MDTs. The advancement in this field allows the development of an affordable and improved method of disease management with avoidance of numerous issues associated to the other delivery systems.

KEYWORDS: *Mouth dissolving tablets, Patient compliance, Dysphagia, Rapid onset of action, Bioavailability, Patented technologies*

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INTRODUCTION

Up to 50–60% of all dosage forms are administered by oral routes. Solid dosage forms are preferred because they are simple to administration, precise dosage, allow for self-medication, reduce pain, and increase patient compliance. However, this dosage form has some drawbacks, including motion sickness (kinetosis), sudden attacks of allergies or coughing, and a lack of hydration but one significant limitation is "Dysphagia," or trouble swallowing. It is estimated that roughly 45% of the population suffers from this. Particularly, the difficulty is experienced by paediatric and geriatric patients. These factors have led to a lot of interest in tablets that can quickly dissolve or disintegrate in the oral cavity. The "oral cavity" has a good permeability because of mucosal lining being relatively less keratinized in the buccal mucosa [1]. Drug absorbed via "oral cavity" directly enters systemic circulation by a jugular vein ensuring, a rapid onset of action, avoidance of first pass metabolism, and drug degradation in gastric region and enzymatic hydrolysis in intestine [2]. An oral dispersible tablet, also referred to as a fast-dissolving tablet, is a commonly used formulation that considers the benefits of the "oral cavity." According to European pharmacopoeia "MDT (Mouth Dissolving Tablet) should dissolve or disintegrate in less than 3 minutes when placed on tongue".

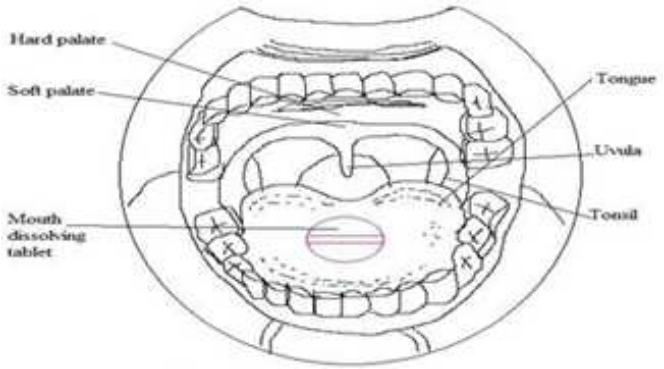

FIG 1: Administration of Mouth Dissolving Tablet

These tablets disintegrate in the mouth within a very short span *i.e.,* 20-30 sec and meets saliva resulting in the therapeutic action of active agent [3,4]. Preparation of mouth dissolving tablet can be manufactured by

several techniques such as Freeze drying or Lyophilization, Spray Drying, Direct Compression, Sublimation, Cotton Candy Process, Mass Extrusion, Molding, Nanonization, Fast Dissolving Films, Phase transition process, Melt granulation.

Mouth dissolving tablets are also known as orally disintegrating tablets, Fast dissolving tablets, Fast melting tablets, etc.

Advantages of Mouth Dissolving Tablet:

- Improved bioavailability and rapid onset of action.
- Requires no water for oral administration, yet dissolve or disintegrate in the mouth in a of seconds.
- Useful for patients who have trouble swallowing dosage forms.
- Compared to oral liquids, an accurate dose can be administered. furthermore, permits high drug loading.
- The tablet's pleasant mouth feel assists paediatric patients in particular to shift their perception of medicine as a bitter pill.
- Solid formulation that can deliver the benefits of a liquid.
- Comparing the drug's stability to oral dosage forms like suspension, it is more stable.
- As unit solid dosage forms, MDT offered excellent stability, precise dosing, ease of manufacture, modest packaging size, and easy to handle by patients.

Disadvantages of Mouth Dissolving Tablet:

- MDT's mechanical strength is its main drawback.
- MDTs are extremely soft and porous moulded matrices that are compressed into tablets with very little force, making the tablets fragile and often needing specialised peeling of blister packing.
- These tablet formulations may not be suitable for patients taking anticholinergic drugs concurrently, those with Sjogren's disease, or those who experience dry mouth as a result of decreased salivation.
- To maintain maximum stability and product security, mouthwash pills require special packaging [5].
- Hygroscopic in nature, MDTs must be stored in a dry atmosphere.

Choice of drug candidate: [6,7]

- No bitter taste.
- Good stability in water and saliva.
- Dose should be low as possible.
- Unsuitable drug candidate for orally disintegrating tablet should include: -
  a. Short half-life and frequent dosing.
  b. Required controlled or sustained release.
  c. Drug having very bitter taste.

Mechanism of mouth dissolving:

Super-disintegrants are given far more consideration when mouth-dissolving tablet formulations are concerned. By inducing swelling and water absorption in the pill, they offer quick disintegration. The super-disintegrants' swelling process wets the carrier's surface, which enhances tablet dissolving and causes higher dissolution rates to occur.

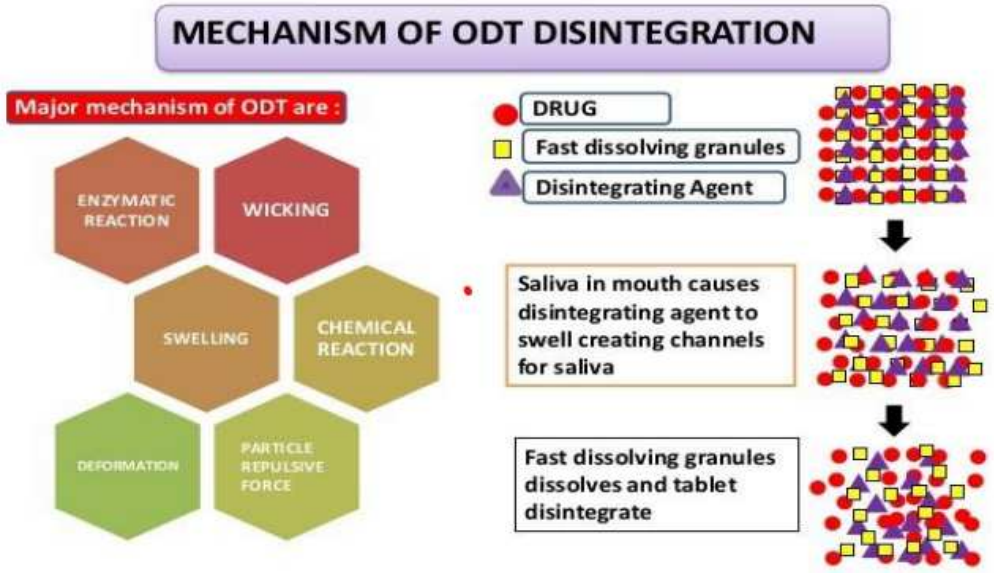

FIG 2: Mechanism of Mouth Dissolving Tablet.

The swelling capacity in the dissolution media and the density of the formed matrix both affect how well super-disintegrants operate. A greater degree of disintegration results from the matrix's higher swelling capacity and density.

Various Technologies Used in Mouth Dissolving Tablet Formulation:

Freeze drying technology:

There is also the word "lyophilization" for it. It can be used to make tablets with an extremely porous open matrix network, allowing saliva to easily pass through it and dissolve the lyophilized mass once it is put in the mouth. To make a unit that dissolves fast in the mouth, the medication is mixed with a freeze-dried, water-soluble matrix. For freeze-drying formulations, low dosage, chemical stability, tiny particle size, and tastelessness are the ideal pharmacological properties. The production procedure is time- and money-consuming.

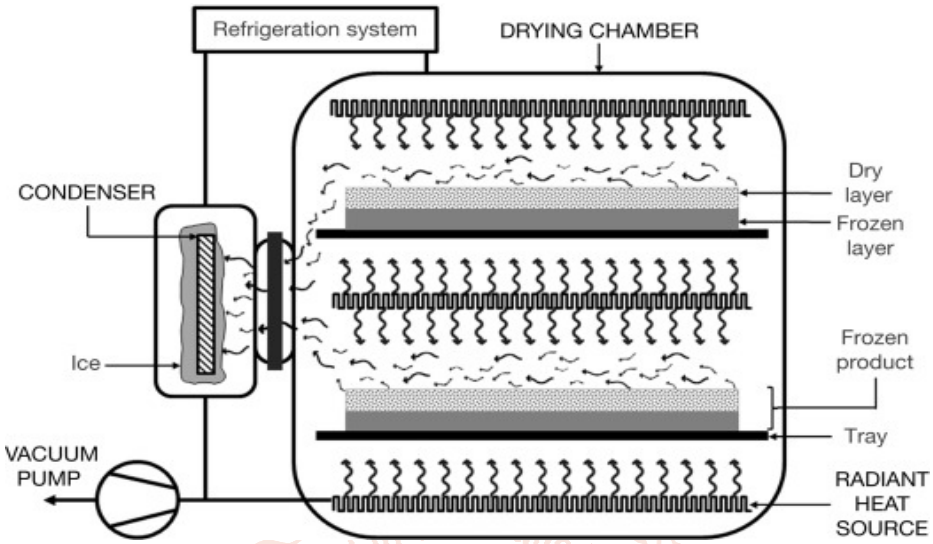

FIG 3: Freeze Dryer Technique

Tablet molding technology:

Molded tablets are made with water-soluble ingredients to enhance rapid medication absorption through the mucosal lining of the mouth. The porous nature of this technology offers the advantage of improving solubility and bioavailability while decreasing first pass metabolism of some medications. To enhance the mouth, feel and tablet breakdown, soluble additives like saccharides are frequently employed in the moulding process. However, handling erosion and breakage are brought on by the moulded tablets' low mechanical strength.

Compression molding:

After being pre-soaked in a solvent like ethanol/water, the powder mixture is pressed onto mould plates to produce a wetted mass.

Heat molding:

A molten matrix that includes a drug that has been dissolved or distributed can be used to create an instantaneous tablet that dissolves in the mouth.

Direct compression method:

The simplest and most economical method of producing tablets is direct compression. It is the method by which tablets are made straight from powder without altering the physical properties of the raw components. It is the simplest technique for compressing tablets. Directly compressible tablets must be cost-effective, have a small number of manufacturing stages, employ ordinary equipment and readily available excipients, and have good flow properties.

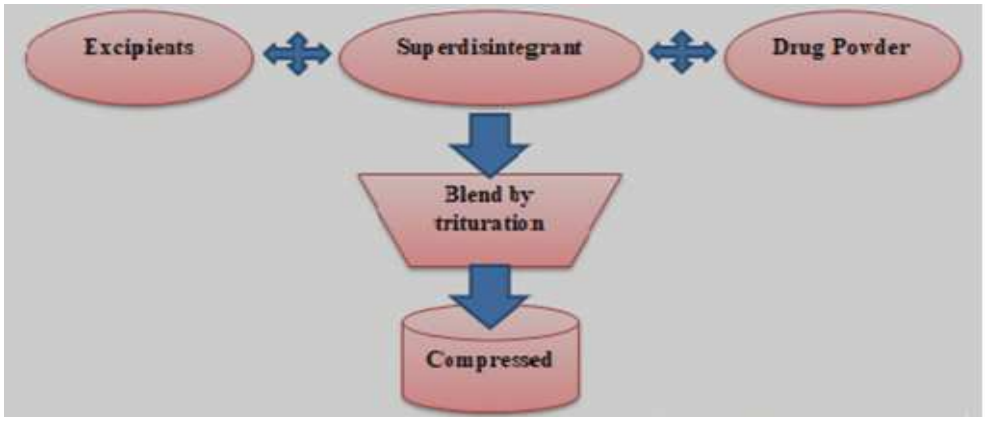

FIG 4: Direct Compression Technique

Spray-drying technology:

The pharmaceutical industry uses a process to create very porous powders technology for spray drying. Quick evaporation of the processing solvent occurs as spray drying, which results in a highly porous product that can be employed to create delectable tablets. Tablets have been seen to have made of spray-dried powder dissolve in water for 20 seconds

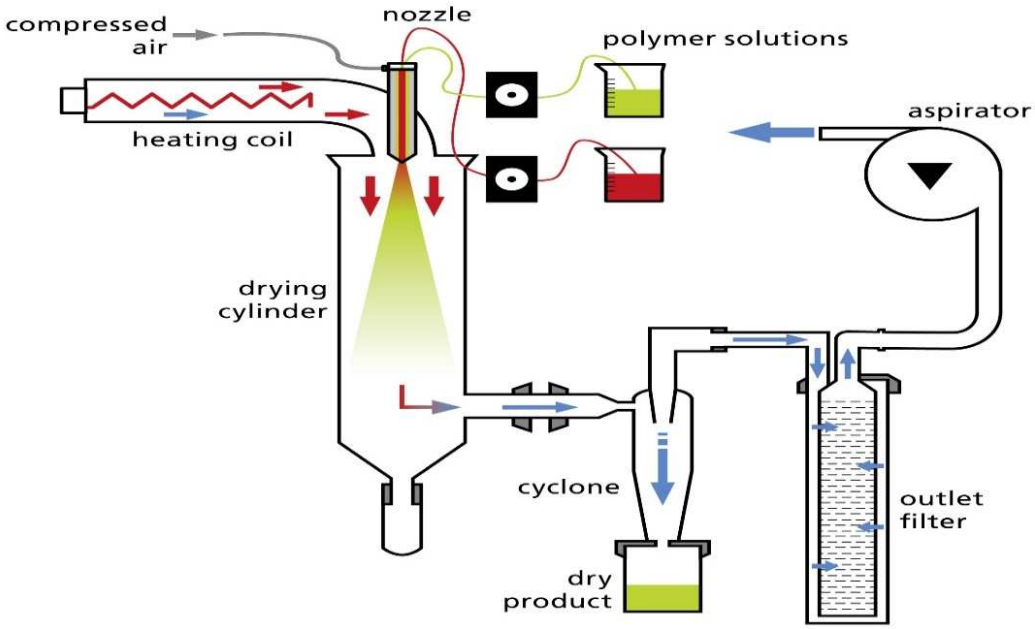

FIG 5: Spray-Drying Technique

Sublimation technology:

The quick breakdown of mouth-dissolved tablets depends on the porosity design of the tablet matrix. Tablets are traditionally compressed, after which the softened substance is forced through an extruder or syringe and cut into uniform pieces by a hot blade. To mask the taste of pharmaceutical grains, a bitter flavour may be added to the dried cylinder [8].

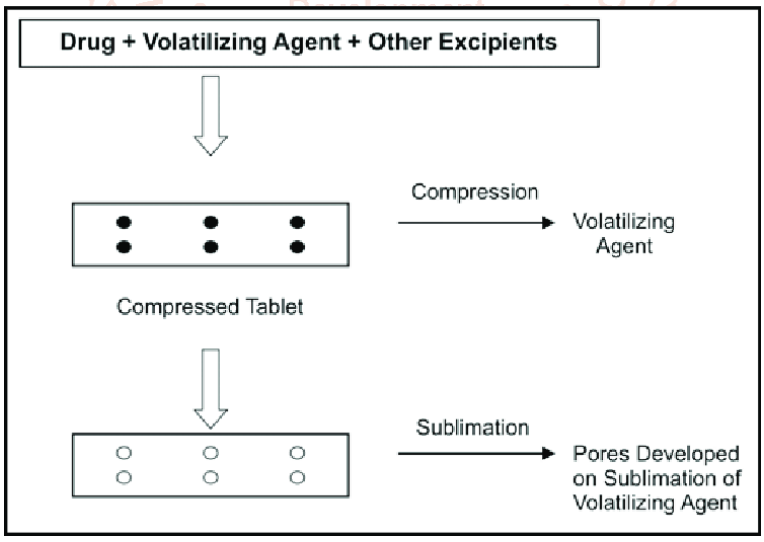

FIG 6: Sublimation Technique

Melt granulation technology:

This technique effectively combines pharmaceutical granules with a meltable binder. This method is better than traditional granulation because it doesn't need organic solvents or water. The technique is speedier and uses less energy than wet granulation because there is no drying stage. It is helpful to speed up the pace at which medications, such as griseofulvin, dissolve in bodily fluids. This method uses a hydrophilic waxy binder, such as superpolystate or PEG-6-stearate, to create MDT with adequate mechanical integrity [9].

Cotton candy process:

It is often referred to as the "sugar floss" strategy. The matrix of the mouth-dissolving pill might either be candy floss- or shear-shaped. Saccharides or polysaccharides that have undergone simultaneous flash melting and centrifugal force processing to produce amorphous floss are used to make the matrix. A material with good flow

and compressibility properties is produced after either partial or total recrystallization of the matrix. The candy floss may then be crushed into MDT after being ground, combined, and blended with the active components and other excipients. Due of the high processing temperature, this method can only be employed with heat stable materials [10].

Nanonization:

Using a novel wet milling method, a recently developed nanomelt technology reduces drug particle size to nano size. Surface adsorption on certain stabilisers, which are then added to MDTs, prevents the drug's nanocrystals from congealing. This method is especially beneficial for medications that are only slightly soluble in water. Two additional advantages of this method are fast nanoparticle dissolution, which boosts absorption, boosts bioavailability, and reduces dose requirements [11].

Patented Techniques for Fast Dissolving Tablets Formulation:

Zydis Technology:

Zydis formulation is a unique technology of preparing fast dissolving tablet. It is freeze dried tablet technology in which drug materials are physically entrapped or dissolved within the matrix of fast dissolving carrier materials. Water is not required for swallowing because when "zydis unit" is put in mouth then the freeze-dried structure disintegrates rapidly. Zydis material is composed of so many substances to achieve a number of objectives [12]. To provide strength during handling polymers such as dextran, alginate and gelatin are incorporated. Saccharides such as sorbitol or mannitol are incorporated to obtain good elegance, hardness and crystallinity. To prevent the shrinkage of "zydis unit" during freeze drying process or long-term storage glycine is generally used as collapse protectants.

Quicksolve:

Similar to Zydis tablets, the solid dosage formulation created using Quicksolve technology is characterised by a porous network. With water, Quicksolve tablets can dissolve within 10 seconds. The excipients employed are xanthan gum, gelatin, pectin, and mannitol (at least 0.5%), as well as matrix-forming agents at concentrations ranging from 0.1% to around 3% w/w. Amino acids, particularly glycine, are used at a concentration at least equivalent to 0.5% w/w. The procedure is distributing gas bubbles into a suspension or solution to create foam. Air, oxygen, nitrogen, and argon are acceptable gases, depending on how well they get along with the system's parts. The resulting foam melts back during the freeze-drying process and is not susceptible to cracking. The primary benefit is quicker, more effective production, which is suitable for drug that are sensitive to heat.

Lyoc:

A water soluble or water dispersible excipient is employed in the manufacture of quickly disintegrating solid oral dosage forms of poorly soluble medicines (solubility between 1 and 30 mg/ml) at a concentration range from 15% to roughly 40% w/w. A nanoparticulate suspension of the drug in the form of crystalline, semi-crystalline, or amorphous particles, or a combination of these, is created in the oral cavity as the oral dose form rapidly disintegrates (within 10 seconds). Chemical precipitation, mechanical grinding, or other appropriate processes can be used to create the drug nanoparticles.

Orasolve technology:

This technique was created by the CIMA lab and is utilised to create oral disintegrating dosage forms. This technique masks the taste of the active medication. Effervescent disintegrating agent is also present. To reduce the amount of time needed for oral dissolving, tablets are manufactured using the direct compression technique at a low compression force. The tablets are produced using standard blenders and tablet presses. The produced tablets are pliable and soft.

Dura solve technology:

CIMA labs have a patented technology called DuraSolv. This technology produces tablets that are made up of the drug, fillers, and a lubricant. The traditional tableting equipment is used to create tablets, which are well-rigid. These are available in standard packaging systems like blisters. For products that only need a small amount of active ingredients, DuraSolv is the right technology.

Wow tab technology:

Yamanouchi Pharmaceutical Co. has a patent on the wow tab technology. WOW stands for waterless. To create a quickly melting, robust tablet, a combination of low mouldability and high mouldability saccharides is used in this procedure. The active substance is combined with a saccharide with low moldability, granulated with a saccharide with high moldability, and compacted into a tablet.

Ora vescent:
The foundation of Ora Vescent technology is disintegration brought on by an effervescent reaction. It is the goal of the Ora Vescent drug delivery system to improve transmucosal absorption. Compared to other fast-dissolving tablets, the disintegration time is greater (10-3 minutes), allowing for absorption on the buccal gingival or sublingual mucosae rather than simple swallowing. Since the reaction produces carbon dioxide, hydrophobic medicines are more likely to be transported over the epithelial membrane.

Flash dose technology:
This technology creates a sugar-based matrix called floss from a combination of excipients, either by themselves or in combination with medications. A new version of Ibuprofen called Nurofen Meltelt is based on the same technology.

Flashtab technology:
This technology, which uses tablets with active ingredients in the form of microcrystals, was invented by Prographarm. The remaining steps are completed using conventional technology.

Sheaform technology:
This technology creates a Sheaform matrix made of prepared floss. A feed shock containing sugar is processed using flash heat to create floss.

Ceform technology:
This technology creates microspheres that contain the active ingredient. Basic requirement of this technology is placing dry powder containing either pure drug or special blend of drug and excipients. The microspheres then mixed and compressed into previously selected oral dosage form.

Nanocrystal Technology:
By reducing particle size and increasing surface area, the method increases dissolving rate. Drug particles (less than 1000 nm in diameter), formed by weight milling the drug ingredient, are known as nano-crystal particles.

Wide range of doses per unit (up to 200 mg of API per unit) are provided by nanocrystal fast dissolving technology. Based on proprietary and patent-protected technology elements, products can be well categorised. improved oral medication pharmacokinetics. Utilizing moisture-resistant active ingredients is economical and cost-effective. Wafers of the lyophilized product are created by mixing water-soluble GRAS (Generally Regarded as Safe) components with medication Nano crystal colloidal dispersions. When working with highly potent or hazardous materials reduction procedures, such granulation, blending, and tableting, they are extremely resilient yet quickly dissolve in very little amounts of water. Due to the low manufacturing loss, this method also makes it possible to create fast-dissolving tablets from modest quantities of drugs [13].

Evaluation Test of Mouth Dissolving Tablet:
General appearance:
General appearance of a tablet depends on its overall aesthetic, visual recognition, and overall "elegance." These include the size, shape, colour, flavour, surface roughness, and physical faults of the tablet.

Tablet Thickness:
Thickness of tablet can be measured using a simple procedure. 10 tablets were taken and their thickness was measured using Vernier callipers.

Weight variation:
Taking 20 tablets at random and weighing each one separately is how the weight variation test is conducted. The average weight of a pill is obtained by dividing the composite weight by twenty. Only two of the individual weights may differ from the average weight by the permitted percentage variation, and no individual weight should deviate by more than twice that amount. The table below contains the details.

Table 1: Weight Variation Specification as Per IP

Sr. No.	Average Weight of Tablet (mg)	% Deviation
1	80 mg or less	±10
2	More than 80 mg but less than 250 mg	±7.5
3	250 mg and above	±5

Hardness:
A tablet's hardness determines how well it can endure mechanical shocks during handling, production, packaging, and shipment. The hardness of the tablets was measured using a Monsanto hardness tester. The

tester's two jaws were placed around the tablet's oblong axis. The measurement at this moment should be 0 kg/cm2. The knob was then rotated while applying constant force until the tablet broke. The hardness of the tablets was indicated as the value at this stage.

Friability:

The Roche Friabilator can be used to determine friability. In a plastic container that rotates at a pace of 25 revolutions per minute and lowers a tablet from a height of 6 inches with each rotation, this gadget treats the tablet to the combined impacts of abrasion and stress. A sample of tablets that have been pre-weighed 100 times is rotated in the friabilator [14]. The friability (F) is calculated using the formula below:

$$\%\text{Friability} = (\text{Initial weight- Final weight /Initial weight}) \times 100$$

Wetting time:

Wetting time and contact angle of the dosage form are correlated. It must be evaluated to shed insight on the characteristics of tablet disintegration; a shorter wetting time indicates a tablet will dissolve more quickly. To do this, a tablet is placed in a tiny Petri dish with an internal diameter of 6.5 cm, 6 ml of water, and the time it takes for the tablet to get completely wet is recorded [15].

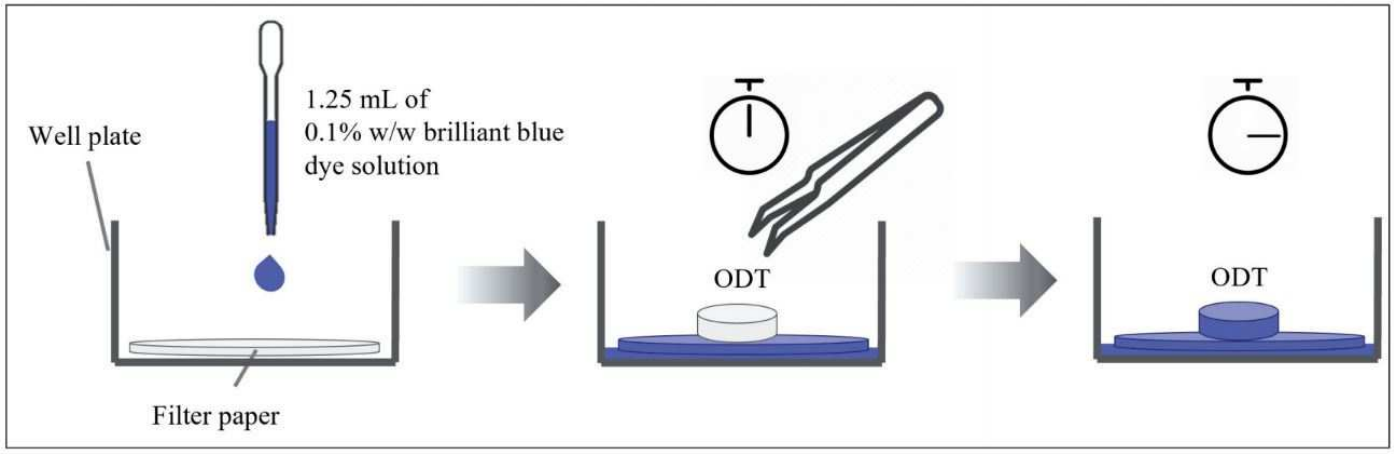

FIG 7: Wetting Time of Mouth Dissolving Tablet.

Disintegration test:

Since fast-dissolving pills must disintegrate without water for the test to be correct, their disintegration times must be altered. For this, a 10 cm diameter Petri dish is filled with 10 ml of water. The duration until the tablet completely crumbles into tiny bits can be seen by placing it gently in the centre of a Petri dish [16].

***In vitro* dispersion time:**

By placing a tablet into a beaker that is filled with 50 ml of liquid, the in vitro dispersion time can be determined. We conduct an in vitro dispersion test by selecting three tablets at random from each formulation. The time it takes for a pill to dissolve entirely can be calculated [17].

In vitro dissolution studies:

The process used to develop dissolution methods for MDTs is comparable to and essentially equivalent to that used for conventional tablets. When scouting runs for a bioequivalent FDT, the dissolution conditions for medications listed in pharmacopoeia monographs are a useful place to start. Other media, such as buffer (pH 4.5 and 6.8) and 0.1 M HCl, should be assessed for MDT in a manner similar to that of their standard tablet counterparts. It has been said that USP 2 paddle apparatus, with a typical paddle speed of 50 rpm, is the most suitable and popular option for orally disintegrating tablets.

Water absorption ratio:

In a little Petri dish filled with 6 mL of water, a piece of tissue paper that had been folded twice was put. The time needed for the tablet to completely wet was measured after a known-weight tablet was placed on the paper. The weighted water absorption ratio R was then calculated for the wet tablet using the following equation.

$R = \{(Wa-Wb) \times 100\}/Wb$

Where, wa = weight of tablet before water absorption;

wb = weight of tablet after water absorption.

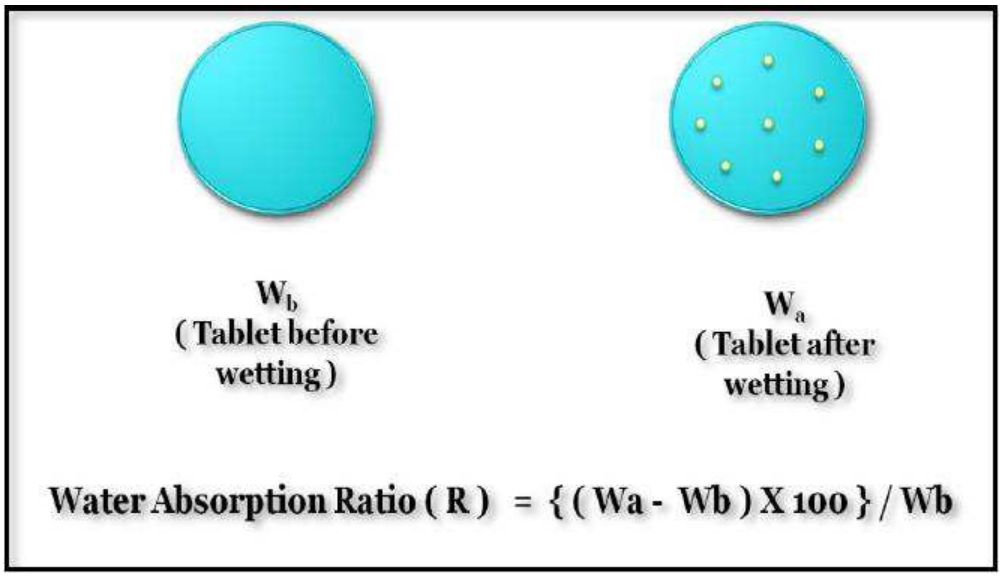

FIG 8: Water Absorption Ratio.

CONCLUSION:

On comparison to more traditional dosage forms like tablets and capsules, mouth-dissolving tablets are highly preferred in the market today. In a drug delivery system, patient compliance and satisfaction are crucial. In addition to being advantageous to dysphasic individuals, mouth-dispersing tablets are cost-effective because they dissolve in the mouth within a few minutes and release active ingredients. The latest manufacturing techniques result in tablets that act quickly, have a higher bioavailability, have less side effects, and are safer.

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CONFLICT OF INTEREST:

All authors declared no conflict of interest for the work.

REFERENCES:

[1] Kumari, S., Visht, S., Sharma, P.K., Yadav, R.K., Fast dissolving Drug delivery system: Review Article; J Pharmacy Research, 2010, 3(6),1444-1449

[2] Bandari, S., Mittapalli, R.K., Gannu, R., Rao, Y.M., Orodispersible tablets: An overview. Asian J Pharm, 2008, 2, 2–11

[3] Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F and Khan A: Orally disintegrating films: A modern expansion in drug delivery system. Saudi Pharmaceutical Journal 2016; 24: 537-46.

[4] Dungarwal UN and Patil SB: Development of orodispersible tablets of taste masked rizatriptan benzoate using hydroxypropyl β-cyclodextrin. Journal of Pharmaceutical Investigation 2016; 46: 537-45.

[5] Masih A, Kumar A, Singh S, Tiwari AK. Fast dissolving tablets: A review. Int J Curr Pharm Res 2017; 9:8-18.

[6] Sunita Kumari, Visht Sharad, Sharma Pramod Kumar, Yadav Rakesh Kumar, Fast dissolving Drug delivery system: Review Article. Journal of Pharmacy Research 2010, 3(6), 1444-1449

[7] Sahoo Susijit, Mishra B., Biswal P.K., Panda Omprakash, Mahapatra Santosh Kumar, Jana Goutam Kumar: Fast Dissolving Tablet: As A Potential Drug Delivery System. Drug Invention Today 2010,2(2),130-133

[8] Rudnic E, Schwartz JB, Tablets, Remington's the Science and Practice of Pharmacy. Oral Solid Dosage Forms. 19th ed., Ch. 92. New York: Marcel Dekker. p. 1615-41.

[9] Shanmugam S. Granulation techniques and technologies: Recent progresses. Bioimpacts 2015; 5:55-63. doi:10.15171/bi.2015.04, PMID 25901297

[10] Aarti J, Sonali J, Ganesh D. Orodispersible tablets: A comprehensive review. Res J Pharm Technol 2014; 7:368-75.

[11] Beri C, Sacher I. Development of fast disintegration tablets as oral drug delivery system-A review. Indian J Pharmacol Biol Res 2013; 1:80-9.

[12] Panigrahi, D., Baghel, S., Mishra, B., Mouth dissolving tablet: An overview of preparation techniques, evalution and patented technologies, J. Pharma. Research, 2005, 4(3), 33-8

[13] Kumar, R. Patil, S., Patil, S.R., Paschapur, M.S., Formulation, evaluation of mouth dissolving tablets of fenofibrate using sublimation technique, Int J Chem Tech Res, 2009, 1(4), 840-850

[14] Prajapati BG, Patel B. Formulation, evaluation and optimization of orally disintegrating tablet of piroxicam. Int J Pharm Tech Res 2010; 2:1893-9.

[15] Manivannan R. Oral disintegrating tablets: A future compaction. Drug Invent Today 2009; 1:61-5.

[16] Mangal M, Thakral S, Goswami M, Thakur N. Comparison study between various reported disintegrating methods for fast dissolving tablets. Afr J Basic Appl Sci 2012; 4:106-9.

[17] Allam A, Fetih G. Sublingual fast dissolving niosomal films for enhanced bioavailability and prolonged effect of metoprolol tartrate. Drug Des Dev Ther 2016; 10:2421-33. doi:10.2147/DDDT.S113775, PMID 27536063

[18] Siddiqui MN, Garg G, Sharma PK. Fast dissolving tablets: preparation, characterization and evaluation: an overview. International Journal of Pharmaceutical Sciences Review and Research. 2010 Sep; 4(2):87-96.

[19] Vinoth R, Sivakrishnan S, Swamivelmanickam M, Tamilselvan C. A Comprehensive Review on Mouth Dissolving Tablet. Journal of Pharmaceutical Research International. 2021 Dec 18:502-13.

[20] Garg A, Gupta MM. Mouth dissolving tablets: a review. Journal of Drug Delivery and Therapeutics. 2013 Mar 15; 3(2).

[21] Kumar P, Usman MR, Sharma A, Mani M, Singh P, Verma N. Mouth Dissolving Tablets: A Modern Approach to Delivery of Drug. Research Journal of Pharmacy and Technology. 2020; 13(6):2943-50.

[22] Masih D, Gupta R. Mouth dissolving tablets–a review. Pharmaceutical and Biosciences Journal. 2013 Nov 14:18-24.

[23] Ashish G, Mahesh M, Sharma Pravin K, Ravi S, Koka Sweta S, Gajanan D. Formulation and evaluation of mouth dissolving tablet of almotriptan malate. Am J PharmTech Res. 2021; 11(05):63-9.

[24] Nagar P, Singh K, Chauhan I, Verma M, Yasir M, Khan A, Sharma R, Gupta N. Orally disintegrating tablets: formulation, preparation techniques and evaluation. Journal of Applied Pharmaceutical Science. 2011 Jun 30(Issue):35-45.

[25] Joshi R, Garud N, Akram W. Fast dissolving tablets: a review. Int J Pharm Sci Res. 2020; 11(4):1562-70.

[26] Khanna K, Xavier G, Joshi SK, Patel A, Khanna S, Goel B. Fast dissolving tablets-A novel approach. International Journal of Pharmaceutical Research & Allied Sciences. 2016 Jan 1; 5(2):311-22.